AMENDMENTS

Please amend the application as set forth below.

In the Claims
Cancel claims 1-17 and add the following new claims 18-33.

18. (new) A compound of the formula I

$$R_a - A - Het - B - Ar - E \qquad (I)$$

wherein

A denotes a carbonyl or sulphonyl group linked to the benzo moiety of the group Het,

B denotes an ethylene group, wherein a methylene group, linked either to the group Het or Ar, is optionally replaced by an oxygen or sulphur atom or by a sulphinyl, sulphonyl, carbonyl or $-NR_1$ group, wherein

R_1 denotes a hydrogen atom or a C_{1-6}-alkyl group,

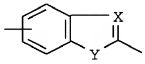
E denotes a cyano or $R_bNH-C(=NH)-$ group wherein

R_b denotes a hydrogen atom, a hydroxy group, a C_{1-3}-alkyl group or a group which is cleaved *in vivo*,

Ar denotes a phenylene or naphthylene group optionally substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, C_{1-3}-alkyl or C_{1-3}-alkoxy group,

or a thienylene group optionally substituted in the carbon skeleton by a C_{1-3}-alkyl group,

Het denotes a bicyclic heterocycle of formula



wherein,

X is a nitrogen atom and

Y is an imino group optionally substituted by a C_{1-6}-alkyl or C_{3-7}-cycloalkyl group

and R_a denotes an R_2NR_3- group wherein

R_2 denotes a C_{1-4}-alkyl group, which is optionally substituted by a carboxy, C_{1-6}-alkyloxycarbonyl, benzyloxycarbonyl, C_{1-3}-alkylsulphonylaminocarbonyl,

phenylsulphonylaminocarbonyl, trifluorosulphonylamino, trifluorosulphonylaminocarbonyl or 1H-tetrazolyl group, or

a C_{2-4}-alkyl group substituted by a hydroxy, phenyl-C_{1-3}-alkoxy, carboxy-C_{1-3}-alkylamino, C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino, N-(C_{1-3}-alkyl)-carboxy-C_{1-3}-alkylamino or N-(C_{1-3}-alkyl)-C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino group, whilst in the abovementioned groups the carbon atom in the α-position relative to the adjacent nitrogen atom may not be substituted, and

R_3 denotes a pyridinyl group optionally substituted by a methyl group,

or a tautomer or salt thereof.

19. (new) A compound of the formula I according to claim 1, wherein

A denotes a carbonyl or sulphonyl group linked to the benzo moiety of the group Het,

B denotes an ethylene group, in which a methylene group, linked either to the group Het or Ar, is optionally replaced by an oxygen or sulphur atom or by a sulphinyl, sulphonyl, carbonyl or -NR_1- group, wherein

R_1 denotes a hydrogen atom or a C_{1-5}-alkyl group,

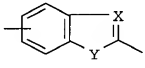
E denotes an R_bNH-C(=NH)- group wherein

R_b denotes a hydrogen atom, a hydroxy group, a C_{1-3}-alkyl group or a group which is cleaved *in vivo*,

Ar denotes a phenylene group optionally substituted by a fluorine, chlorine or bromine atom or by a trifluoromethyl, C_{1-3}-alkyl or C_{1-3}-alkoxy group,

or a thienylene group optionally substituted in the carbon skeleton by a C_{1-3}-alkyl group,

Het denotes a bicyclic heterocycle of formula



wherein,

X is a nitrogen atom and

Y is an imino group optionally substituted by a C_{1-6}-alkyl or C_{3-7}-cycloalkyl group

and R_a denotes a R_2NR_3- group wherein

R_2 denotes a C_{1-4}-alkyl group, which is optionally substituted by a carboxy, C_{1-6}-alkyloxycarbonyl, benzyloxycarbonyl, C_{1-3}-alkylsulphonylaminocarbonyl, phenylsulphonylaminocarbonyl, trifluorosulphonylamino, trifluorosulphonylaminocarbonyl or 1H-tetrazolyl group, or

a C_{2-4}-alkyl group substituted by a hydroxy, phenyl-C_{1-3}-alkoxy, carboxy-C_{1-3}-alkylamino, C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino, N-(C_{1-3}-alkyl)-carboxy-C_{1-3}-alkylamino or N-(C_{1-3}-alkyl)-C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino group, whilst in the abovementioned groups the carbon atom in the α-position relative to the adjacent nitrogen atom may not be substituted, and

R_3 denotes pyridinyl group optionally substituted by a methyl group,

or a tautomer or salt thereof.

20. (new) A compound of the formula I according to claim 1, wherein

A denotes a carbonyl or sulphonyl group linked to the benzo moiety of the group Het,

B denotes an ethylene group in which the methylene group linked to the group Ar is optionally replaced by an oxygen or sulphur atom or by an -NR_1- group, wherein

R_1 denotes a hydrogen atom or a C_{1-4}-alkyl group,

E denotes an R_bNH-C(=NH)- group wherein

R_b denotes a hydrogen atom, a hydroxy, C_{1-9}-alkoxycarbonyl, cyclohexyloxycarbonyl, phenyl-C_{1-3}-alkoxycarbonyl, benzoyl, p-C_{1-3}-alkyl-benzoyl or pyridinoyl group, whilst the ethoxy moiety in the 2-position of the abovementioned C_{1-9}-alkoxycarbonyl group is optionally, additionally, substituted by a C_{1-3}-alkyl-sulfonyl or 2-(C_{1-3}-alkoxy)-ethyl group,

Ar denotes a 1,4-phenylene group optionally substituted by a chlorine atom or by a methyl, ethyl or methoxy group or it denotes a 2,5-thienylene group,

Het denotes a 1-(C_{1-3}-alkyl)-2,5-benzimidazolylene or 1-cyclopropyl-2,5-benzimidazolylene group and

R_a denotes an R_2NR_3- group wherein

R_2 is a C_{1-4}-alkyl group substituted by a carboxy, C_{1-6}-alkyloxycarbonyl, benzyloxycarbonyl, C_{1-3}-alkylsulphonylaminocarbonyl or 1H-tetrazol-5-yl group, or

a C_{2-4}-alkyl group substituted by a hydroxy, benzyloxy, carboxy-C_{1-3}-alkylamino, C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino, N-(C_{1-3}-alkyl)-carboxy-C_{1-3}-alkylamino or N-(C_{1-3}-alkyl)-C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino group, whilst in the

abovementioned groups the carbon atom in the α-position to the adjacent nitrogen atom may not be substituted, and

R_3 denotes a pyridinyl group optionally substituted by a methyl group,

or a tautomer or salt thereof.

21. (new) A compound of the formula I according to claim 1, wherein

A denotes a carbonyl or sulphonyl group linked to the benzo moiety of the group Het,

B denotes an ethylene group in which the methylene group linked to the group Ar is optionally replaced by an oxygen or sulphur atom or by an $-NR_1-$ group, wherein

R_1 denotes a hydrogen atom or a methyl group,

E denotes an $R_bNH-C(=NH)-$ group, wherein

R_b denotes a hydrogen atom or a hydroxy, C_{1-9}-alkoxycarbonyl, cyclohexyloxycarbonyl, benzyloxycarbonyl, benzoyl, p-C_{1-3}-alkylbenzoyl or nicotinoyl group, whilst the ethoxy moiety in the 2-position of the abovementioned C_{1-9}-alkoxycarbonyl group is optionally, additionally, substituted by a C_{1-3}-alkylsulphonyl or 2-(C_{1-3}-alkoxy)-ethyl group,

Ar denotes a 1,4-phenylene group optionally substituted by a chlorine atom or by a methyl, ethyl or methoxy group, or it denotes a 2,5-thienylene group,

Het denotes a 1-methyl-2,5-benzimidazolylene or 1-cyclopropyl-2,5-benzimidazolylene group and

R_a denotes a R_2NR_3- group wherein

R_2 denotes a C_{1-3}-alkyl group which is optionally substituted by a carboxy, C_{1-6}-alkyloxycarbonyl, benzyloxycarbonyl, methylsulphonylaminocarbonyl or 1H-tetrazol-5-yl group, or

a C_{2-3}-alkyl group substituted by a hydroxy, benzyloxy, carboxy-C_{1-3}-alkylamino, C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino, N-(C_{1-3}-alkyl)-carboxy-C_{1-3}-alkylamino or N-(C_{1-3}-alkyl)-C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino group, whilst in the abovementioned groups the carbon atom in the α-position to the adjacent nitrogen atom may not be substituted, and

R_3 denotes a pyridinyl group,

or a tautomer or salt thereof.

22. (new) A compound of the formula I according to claim 1, wherein

A denotes a carbonyl group linked to the benzo moiety of the group Het,

B denotes an ethylene group wherein the methylene group attached to the group Ar is optionally replaced by an -NR_1 group, whilst

R_1 denotes a hydrogen atom or a methyl group,

E denotes an R_bNH-C(=NH)- group wherein

R_b is a hydrogen atom, a hydroxy, C_{1-9}-alkoxycarbonyl, cyclohexyloxycarbonyl, benzyloxycarbonyl, benzoyl, p-C_{1-3}-alkyl-benzoyl or nicotinoyl group, whilst the ethoxy moiety in the 2-position of the abovementioned C_{1-9}-alkoxycarbonyl group is optionally, additionally, substituted by a methylsulfonyl or 2-ethoxy-ethyl group,

Ar denotes a 1,4-phenylene group optionally substituted by a methoxy group or it denotes a 2,5-thienylene group,

Het denotes a 1-methyl-2,5-benzimidazolylene group and

R_a denotes an R_2NR_3- group wherein

R_2 denotes a C_{1-3}-alkyl group which is optionally substituted by a carboxy, C_{1-6}-alkyloxycarbonyl, benzyloxycarbonyl, methylsulfonylaminocarbonyl or 1H-tetrazol-5-yl group, or

a C_{2-3}-alkyl group substituted by a hydroxy, benzyloxy, carboxy-C_{1-3}-alkylamino, C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino, N-(C_{1-3}-alkyl)-carboxy-C_{1-3}-alkylamino or N-(C_{1-3}-alkyl)-C_{1-3}-alkoxycarbonyl-C_{1-3}-alkylamino group, whilst in the abovementioned groups the carbon atom in the α-position to the adjacent nitrogen atom may not be substituted, and

R_3 denotes
a 2-pyridinyl group,

or a tautomer or salt thereof.

23. (new) A compound selected from the group consisting of:

(a) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(hydroxycarbonylmethyl)-amide,

(b) 1-Methyl-2-[2-(2-amidinothiophen-5-yl)ethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,

(c) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,

(d) 1-Methyl-2-[2-(4-amidinophenyl)ethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,

(e) 1-Methyl-2-[N-(4-amidinophenyl)-N-methyl-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,

(f) 1-Methyl-2-[N-(4-amidinophenyl)-N-methyl-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(3-pyridyl)-N-(2-hydroxycarbonylethyl)-amide and

(g) 1-Methyl-2-[N-(4-amidino-2-methoxy-phenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide,

or a prodrug, double prodrug or physiologically acceptable salt thereof.

24. (new) 1-Methyl-2-[N-(4-amidinophenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide or a prodrug, double prodrug or physiologically acceptable salt thereof.

25. (new) 1-Methyl-2-[N-(4-amidino-2-methoxy-phenyl)-aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-hydroxycarbonylethyl)-amide, or a prodrug, double prodrug or physiologically acceptable salt thereof.

26. (new) 1-Methyl-2-[N-[4-(N-n-hexyloxycarbonylamidino)phenyl]aminomethyl]-benzimidazol-5-yl-carboxylic acid-N-(2-pyridyl)-N-(2-ethoxycarbonylethyl) amide or a physiologically acceptable salt thereof.

27. (new) A physiologically acceptable salt of a compound according to claim 18, 19, 20, 21 or 22, wherein E denotes an R_bNH-C(=NH)- group.

28. (new) A pharmaceutical composition containing a compound according to claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein E denotes an R_bNH-C(=NH)- group, or a physiologically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

29. (new) A method for preventing or treating venous and arterial thrombotic disease which comprises administering an antithrombotic amount of a compound according claim 18, 19, 20, 21, 22, 23, 24, 25 or 26, wherein E denotes an R_bNH-C(=NH)- group, or a physiologically acceptable salt thereof.